Enantio- and Diastereo-selective Synthesis of Spirocyclic Compounds

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Spirocyclic diones such as (*R*)-spiro[4.4]nonane-1,6-dione **1a**, (*R*)-spiro[4.5]decane-1,6-dione **1b** and (*R*)-spiro[5.5]undecane-1,7-dione **1c**, and the corresponding *cis,cis*-diols **2a–c** have been enantio- and diastereo-selectively synthesized by asymmetric alkylation and reduction using C_2-symmetric cycloalkane-1,2-diols as a chiral auxiliary.

Optically active spirocyclic diones such as spiro[4.4]nonane-1,6-dione **1a**, spiro[4.5]decane-1,6-dione **1b** and spiro[5.5]-undecane-1,7-dione **1c** are compounds of interest in the area of chiral homoconjugation.[1] Furthermore, the corresponding *cis,cis*-diols **2a–c**[2] are considered to be promising compounds as a new type of chiral auxiliary.

In an earlier paper, we reported a new method for preparing compounds containing a chiral quaternary carbon utilizing cycloalkane-1,2-diols as a chiral auxiliary.[3] As a synthetic application of this asymmetric alkylation, we here report the synthesis of (*R*)-**1a–c** and (1*R*,5*R*,6*R*)-spiro[4.4]nonane-1,6-diol **2a** (1*R*,5*R*,6*R*)-spiro[4.5]decane-1,6-diol **2b** and (1*R*,6*R*,7*R*)-spiro[5.5]undecane-1,7-diol **2c**, in a highly enantio- and diastereo-selective manner (Fig. 1).

Our proposed synthetic route to the target molecules is shown in Scheme 1. We planned to prepare the first synthetic intermediate **A**, containing a quaternary carbon, by two types of asymmetric alkylation utilizing the chiral acetal **3** or the tricyclic lactone **5** along the lines of our earlier work.[3] Dieckmann condensation of **A** and subsequent dealkoxycarbonylation might then afford the second intermediate **B**, removal of the acetal function from which should afford the diketones **1a–c**. Furthermore, diastereoselective two-step reductions of **B** would then, it was thought, afford the desired *cis*, *cis*-diols **2a–c**.†

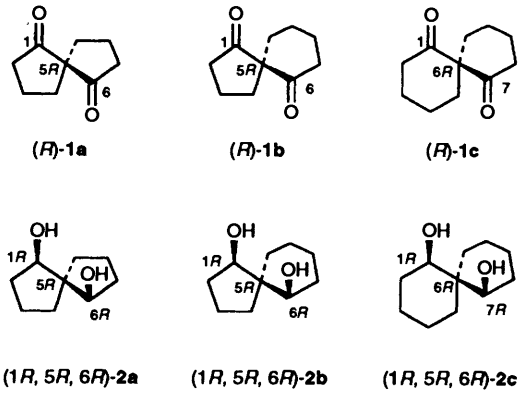
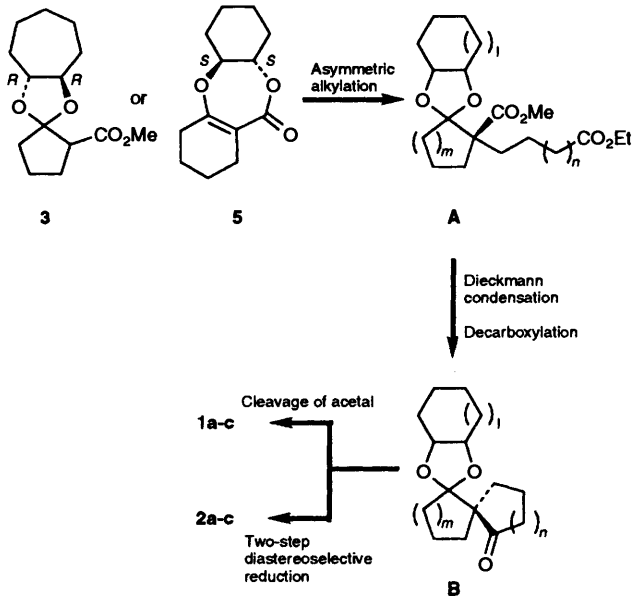


Fig. 1

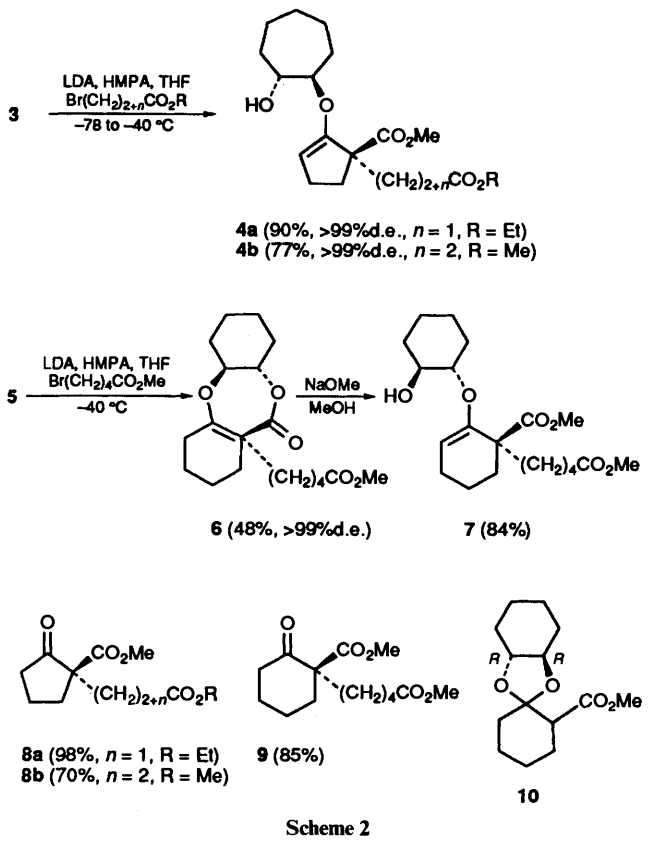


Scheme 1

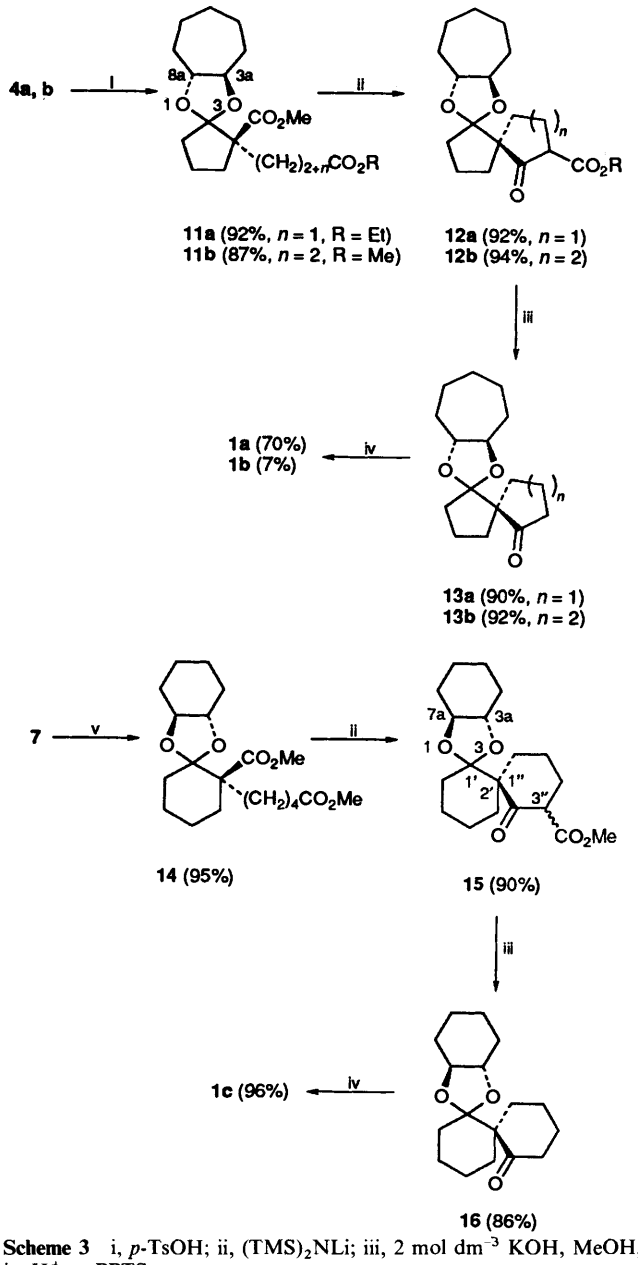
Preparation of the Quaternary Carbon-containing Intermediate.—Asymmetric alkylation of the chiral acetal **3** derived from a 5-membered β-keto ester and (*R*,*R*)-cycloheptane-1,2-diol, with ethyl 4-bromobutyrate and methyl 5-bromopentanoate afforded the alkylated enol ethers **4a** (90%) and **4b** (77%), respectively, in a completely diastereoselective manner (> 99% d.e.). In contrast, a similar alkylation of the six-membered compound **10** with methyl 5-bromopentanoate afforded a complex mixture. This was thought to be the result of a competitive reaction; *i.e.*, conversion of compound **10** into a tricyclic lactone (*ent*-**5**) under the basic conditions employed and subsequent alkylation occurred with reverse diastereoselectivity. This unwanted reaction was considered to be attributable to the slow rate of alkylation of **10**.[3d] An alternative synthetic approach to the alkylated enol ether **7** was achieved in a two-step sequence, namely by alkylation of **5** to give **6** (48%, > 99% d.e.) and subsequent lactone ring-opening of the latter with NaOMe to afford **7** (84%). The d.e. of **4a**, **b** and **7** were determined by 270 MHz ^{1}H NMR spectroscopy in the presence of (+)-Eu(hfc)$_3$ after their conversion into the corresponding ketones **8a**, **b** and **9**, respectively. Based on our previous mechanistic consideration,[3c,d] the newly generated quaternary carbons were expected to have the absolute configuration depicted in Scheme 2. Absolute configurations of **4a**, **b** were finally confirmed by conversion into the configurationally known spirocyclic diketones **1a**, **b**, respectively.

Synthesis of Spirocyclic Diketones.—The enol ethers **4a**, **b** and **7** were easily converted into the corresponding acetals **11a**, **b** and **14**, respectively, by acid treatment in 87–95% yields. Subsequent Dieckmann condensation with lithium bis(trimeth-

† In previous synthetic studies, for example, compound **1a** and **2a** were resolved by Gerlach[4a] and Shingu[4b] based on repeated recrystallization after conversion into a diastereoisomeric mixture of optically active camphanate derivatives.



Scheme 2



Scheme 3 i, *p*-TsOH; ii, $(TMS)_2NLi$; iii, 2 mol dm^{-3} KOH, MeOH; iv, H^+; v, PPTS

ylsilyl)amide in THF at room temperature successfully afforded the spirocyclic β-keto esters **12a**, **b** and **15**, respectively, in 90–94% yields as a mixture of diastereoisomers at the α-position of the ester function. Use of Bu^{t}OK instead of lithium bis(trimethylsilyl)amide gave compound **12a** in 60% yield from **11a**. Subsequent dealkoxycarbonylation of **12a**, **b** and **15** with 2 mol dm^{-3} aqueous KOH in MeOH gave the corresponding keto acetals **13a**, **b** and **16**, respectively, in 86–92% yields (Scheme 3).

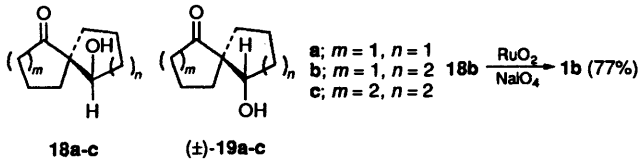
Deacetalization of the keto acetals **13a**, **b** and **16** was carefully studied, since competitive paths such as a retro-aldol reaction and Grob's type fragmentation were possible with these β-keto acetal systems in acidic media. Preliminary reactions were performed under the following conditions: (a) 3.5% aqueous HCl–acetone, room temp.; (b) BF_3·Et_2O–H_2O–acetone, room temp.; (c) $ZnBr_2$–CH_2Cl_2–THF, room temp. The behaviour of substrates under these conditions differed one from another and depended on the skeletal stability of each. Compound **13a** with a spiro[4.4]nonane skeleton afforded the corresponding diketone **1a** as a major product under conditions of (a)–(c) accompanied by several by-products (TLC). Of these conditions, (c) was found to be the best, affording the desired compound **1a** in 70% yield. Compound **16** with spiro[5.5]undecane skeleton gave **1c** as a single product under conditions of (a)–(c). Reaction under (a) was fastest and afforded **1c** in 96% yield.

In contrast to the stability of **1a** and **1c**, compound **13b** with a spiro[4.5]decane skeleton afforded a complex mixture under the conditions of (a)–(c). Conditions (a) gave **1b** in only 7% yield (Scheme 3). An alternative synthetic approach to prepare **1b** from **13b** was successful, proceeding *via* the hydroxy ketone **18b** (details are given in the next section).

Synthesis of Spirocyclic cis,cis-*Diols.*—The enantio- and diastereo-selective synthesis of the *cis,cis*-diols **2a–c** from the keto acetals **13a**, **b** and **16** *via* the hydroxy ketones **18a–c** was studied. For this purpose, a stepwise reduction was considered to be favourable, since the *re*-face of the carbonyl function in **13a**, **b** and **16** was highly shielded by the acetal function. Therefore, reduction might preferentially take place from the less hindered *si*-face.*

Initially, the diastereoselectivity on reduction with $LiAlH_4$ at 0 °C was studied with the racemic substrates (±)-**13a**, **b** and (±)-**16**; they failed to give satisfactory results (the diastereoisomeric ratio was 1:1–5:1). Reduction of **13a**, **b** with bulky DIBAL-H at −78 °C afforded the desired compounds **17a**, **b** of >99% d.e. in 97 and 76% yields, respectively. Reduction of **16** with DIBAL-H at −20 °C failed to proceed, and that with $LiAlH_4$ at −50 °C afforded **17c** of 96% d.e. in 94% yield. Deacetalization of **17a–c** was achieved with 3.5% aqueous HCl–

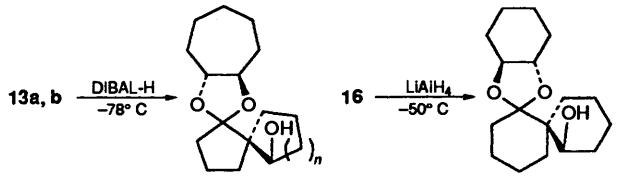
* According to Cram *et al.*[5] reduction of (±)-**1a** with $LiAlH_4$ afforded a mixture of *cis,cis*-, *cis,trans*- and *trans,trans*-diols in a low diastereoselective manner. Recently, Keay[6] *et al.* have reported highly diastereoselective reduction of (±)-**1a** to (±)-**2a** using lithium *tert*-butyldiisobutylaluminium hydride and subsequent resolution using (+)-camphor.



18a-c (±)-19a-c

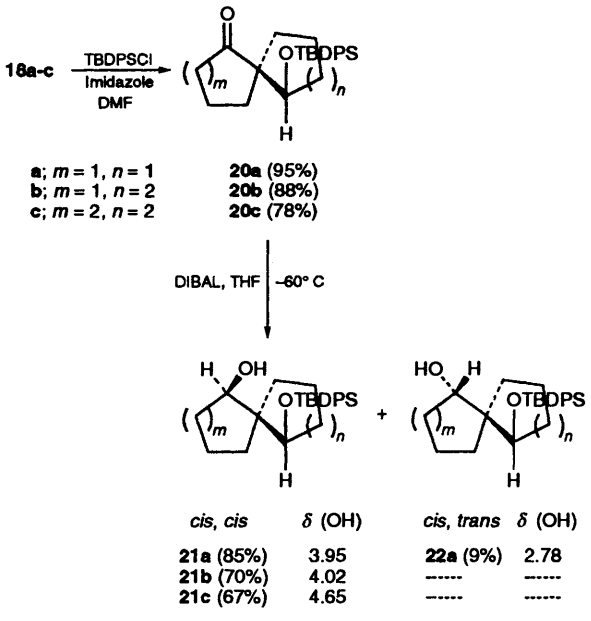
Table 1 Chemical shifts of hydroxy protons (δ)

18a	3.44	(±)-**19a**	2.29
18b	3.78	(±)-**19b**	in 1.22–2.41
18c	3.21	(±)-**19c**	2.41



17a (98%, >99% d.e., n = 1)
17b (85%, >99% d.e., n = 2)
17c (96%, 96% d.e.)

Scheme 4



Scheme 5

acetone at room temperature, affording the hydroxy ketones **18a–c** in quantitative yields. A small amount of **19c** in **18c** could be removed by silica-gel column chromatography.

The diastereoisomeric excess of **17** was determined from the isolated yields of **18** and **19**. The stereochemistry of compounds **18a–c** was determined by comparing the chemical shifts of the hydroxy proton in their ^{1}H NMR spectra with those of (±)-**19**; they could be divided into two types as shown in Table 1. One group observed at lower chemical shifts (δ 3.21–3.78) was assigned to the compound of *cis* configuration, **18**, because of the likely presence of intramolecular hydrogen bonding with the carbonyl function. The other group observed at higher chemical shifts (δ 2.29–2.41) was assigned to the compound of *trans* configuration, **19**.

One of the target molecules **1b** was easily synthesized by neutral oxidation of **18b** with RuO_2–$NaIO_4$ in 77% yield.

In the attempted preparation of *cis*, *cis*-diols, direct reduction of the hydroxy ketone **18** failed to give a satisfactory result. For example, DIBAL-H reduction of **18a** at −60 °C afforded a 1:2 mixture of the *cis,cis*-diol **2a** and the *cis,trans*-diol (**22a** type) in 77% yield. Next, we planned the following sequence of reactions: (i) protection of the hydroxy group as a bulky *tert*-butyldiphenylsilyl ether; (ii) *si*-face selective reduction of the carbonyl function; (iii) deprotection of the silyl ether. The TBDPS ethers **20a–c** were obtained in 78–95% yields from **18a–c** by the usual procedure. As expected, reduction of **20a–c** with DIBAL-H at −78 °C proceeded in a highly *si*-face selective manner to afford **21a-c** with a *cis,cis*-configuration. In the case of the reduction of **20a**, *cis,cis*-**21a** was obtained in 85% yield accompanied with diastereoisomeric **22a** in 9% yield; these were easily separated by silica-gel column chromatography. The same reduction of **20b, c** gave *cis,cis*-**21b, c** in 70 and 67% yields, respectively, in a completely diastereoselective manner. Deprotection of the TBDPS ether in **21a–c** with tetrabutylammonium fluoride (TBAF) quantitatively afforded the corresponding diols **2a–c** (97–99% yields). The stereochemistry of the reduction was deduced in a similar manner to that described for the hydroxy ketones **18** and **19**. That is to say, in the 270 MHz ^{1}H NMR spectra, the hydroxy protons of **21a–c** were observed at lower chemical shifts (δ 3.95–4.65), a result, perhaps, of intramolecular hydrogen bonding with the ether oxygen. The structures of compounds **21a, c** were also determined by comparing their ^{1}H and ^{13}C NMR spectra with those of **2a, c**, in which C_2-symmetrical properties were observed. For example, the ^{13}C NMR spectrum of **2a** showed C-1, -6 at δ 79.6 (3°), C-2, -7, C-3 -8, C-4, -9 at δ 34.3, 33.9, 21.2 (each 2°), and quaternary C-5 at δ 58.3. In its ^{1}H NMR spectrum, 2-H and 6-H were observed as an equivalent signal at δ 4.14.

Thus, three types of spirocyclic skeleton have been enantio- and diastereo-selectively synthesized by a procedure which may provide a general method for the asymmetric synthesis of spirocyclic and related compounds.

Experimental

IR spectra were measured with a JASCO A-202 spectrometer and ^{1}H and ^{13}C NMR spectra were recorded on a JEOL JNM-GX-270 or JEOL JNM-FX-100 spectrometer. Mass spectra (MS) were taken on a JEOL JMS-D 300 spectrometer. Optical rotations were measured on a JASCO DIP-360 polarimeter at the sodium line; values are recorded in units of 10^{-1} deg cm^2 g^{-1}. For column chromatography, silica gel (Merck, Kieselgel 60, 70–230 mesh) was used.

General Procedure for Asymmetric Alkylation of the Acetal **3**.—A solution of BuLi (15% hexane solution; 5 cm^3, 8 mmol) was added dropwise to a stirred solution of diisopropylamine (808 mg, 8 mmol) in THF (25 cm^3) at −78 °C under an Ar atmosphere. After 10 min, HMPA (3.6 g, 20 mmol) in THF (3 cm^3) and substrate **3** [3d] (1.02 g, 4 mmol) in THF (5 cm^3) were added to the mixture which was then stirred for 10 min; alkyl halide (4 mmol) in THF (3 cm^3) was then added to it. After being stirred for 1 h at −78 °C and for additional 24 h at −40 °C, the reaction mixture was diluted with aqueous saturated NH_4Cl, and extracted with ethyl acetate. The extracts were washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by silica gel column chromatography. The fraction eluted with hexane–ethyl acetate (20:1–10:1) afforded **4a, b** as colourless oils.

Methyl (1S)-1-(3-*ethoxycarbonylpropyl*)-2-[(1R,2R)-2-*hydroxycycloheptyl*]*oxycyclopent*-2-*enecarboxylate* **4a**: 90% yield; >99% d.e. $[\alpha]_D^{23}$ −48.3 (*c* 1.2 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 3500 (OH), 1738br (C=O) and 1650 (double bond); δ_H(270 MHz; $CDCl_3$) 4.56 (1 H, t, *J* 3), 4.12 (2 H, q, *J* 7), 3.77–3.61 (2 H, m), 3.69 (3 H, s), 3.48 (1 H, br s), 2.39–2.26 (5 H, m), 2.01–1.83 (4 H, m), 1.77–1.45 (11 H, m) and 1.26 (3 H, t, *J* 7); δ_C(100 MHz; $CDCl_3$) 175.9 (s), 173.3 (s), 156.5 (s), 97.2 (d), 86.7 (d), 75.5

(d), 60.2 (t), 57.7 (s), 52.1 (q), 34.7 (t), 34.5 (t), 32.5 (t), 31.5 (t), 28.4 (t), 27.3 (t), 26.4 (t), 22.3 (t), 22.2 (t), 20.1 (t) and 14.3 (q); *m/z* 368 (M^+, 17%), 267 (14), 254 (11) and 167 (100).

Methyl (1S)-1-(3-*methoxycarbonylbutyl*)-2-[(1R,2R)-2-*hydroxycycloheptyloxy*]*cyclopent*-2-*enecarboxylate* **4b**: 77% yield; >99% d.e. $[\alpha]_D^{22}$ −50.5 (*c* 0.5 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 3500 (OH), 1740br (C=O) and 1650 (double bond); δ_H(270 MHz; $CDCl_3$) 4.54 (1 H, t, *J* 3), 3.75–3.60 (2 H, m), 3.69 (3 H, s), 3.66 (3 H, s), 3.50 (1 H, br s), 2.37–2.21 (5 H, m) and 1.96–1.18 (17 H, m); δ_C(100 MHz; $CDCl_3$) 176.1 (s), 174.0 (s), 156.7 (s), 97.1 (d), 86.6 (d), 75.7 (d), 57.9 (s), 52.1 (q), 51.4 (q), 34.9 (t), 33.9 (t), 32.5 (t), 31.5 (t), 28.4 (t), 27.3 (t), 26.4 (t), 25.3 (t), 24.0 (t), 22.4 (t) and 22.2 (t); *m/z* (EI) 368 (M^+, 19%), 267 (22) and 167 (100).

(3S,8S,11S)-11-(4-*Methoxycarbonylbutyl*)-2,9-*dioxatricyclo*-[9.4.0.0^{3,8}]*pentadec*-1(15)-*en*-10-*one* **6**.—A solution of BuLi (15% hexane solution; 4.8 cm^3, 7.7 mmol) was added dropwise to a stirred solution of diisopropylamine (778 mg, 7.7 mmol) in THF (35 cm^3) at −78 °C under an Ar atmosphere. After 10 min, HMPA (12.5 g, 70 mmol) and the lactone **5** [3c] (1.55 g, 7 mmol) in THF (5 cm^3) were added to the mixture which was then stirred for 10 min; methyl 5-bromovalerate (1.5 g, 7.7 mmol) in THF (3 cm^3) was then added to it. After being stirred for 1 h at −78 °C and for an additional 24 h at −40 °C, the reaction mixture was diluted with aqueous saturated NH_4Cl, and extracted with ethyl acetate. The extracts were washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel. The fraction eluted with hexane–ethyl acetate (10:1) afforded the title compound **6** (1.13 g, 48%) as a colourless oil; $[\alpha]_D^{27}$ +17.7 (*c* 0.3 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 1730 br (C=O) and 1665 (double bond); δ_H(270 MHz; $CDCl_3$) 5.37 (1 H, t, *J* 3), 4.43 (1 H, m), 3.89 (1 H, m), 3.65 (3 H, s), 2.34–2.28 (2 H, m) and 2.17–1.15 (20 H, m); δ_C(100 MHz; $CDCl_3$) 174.9 (s), 174.0 (s), 149.2 (s), 116.7 (d), 81.6 (d), 76.9 (d), 51.4 (s), 51.4 (q), 39.9 (t), 33.9 (t), 33.5 (t), 31.2 (t), 31.2 (t), 25.4 (t), 24.6 (t), 23.6 (t), 23.6 (t), 23.5 (t) and 18.5 (t); *m/z* (EI) 336 (M^+, 6.3%), 308 (89), 150 (86), 141 (100); *m/z* 336.1930 (M^+; Calc. for $C_{19}H_{28}O_5$: 336.1937).

Methyl (1S)-2-[(1S,2S)-2-*Hydroxycyclohexyloxy*]-1-(4-*methoxycarbonylbutyl*)*cyclohex*-2-*enecarboxylate* **7**.—To a solution of NaOMe prepared from Na (230 mg, 10 mmol) in MeOH (30 cm^3) was added compound **6** (1 g, 3 mmol) under an Ar atmosphere. The mixture was stirred at room temperature for 1 h and then diluted with saturated aqueous NH_4Cl (20 cm^3), and extracted with ethyl acetate. The extracts were dried ($MgSO_4$) and concentrated under reduced pressure to afford an oily residue, which was purified by silica gel column chromatography. The fraction eluted with hexane–ethyl acetate (7:1) afforded **7** (920 mg, 84%) as a colourless oil; $[\alpha]_D^{26}$ −6.5 (*c* 0.7 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 3540 (OH), 1730br (C=O) and 1665 (double bond); δ_H(270 MHz; $CDCl_3$) 4.89 (1 H, t, *J* 4), 3.74 (1 H, m), 3.66 (3 H, s), 3.66 (3 H, s), 3.57 (1 H, m), 2.53 (1 H, br s), 2.36–2.30 (2 H, m) and 2.21–1.03 (20 H, m); δ_C(100 MHz; $CDCl_3$) 176.2 (s), 174.2 (s), 151.8 (s), 98.1 (d), 79.2 (d), 73.1 (d), 51.7 (q), 51.5 (q), 50.4 (s), 34.7 (t), 33.8 (t), 32.2 (t), 32.2 (t), 28.0(t), 25.4 (t), 24.2 (t), 23.9 (t), 23.9 (t), 23.7 (t), 19.5 (t); *m/z* (EI) 368 (M^+, 24%), 210 (20) and 156 (100).

General Procedure for Deprotection of the Enol Ethers **4a**, **b** *and* **7**.—To a mixture of BF_3·OEt_2 (0.5 cm^3, 4 mmol) and water (0.5 cm^3) was added a solution of the enol ether (0.2 mmol) in MeOH (4 cm^3) at room temp. The reaction mixture was heated at 60–70 °C for 0.5–3 h and then diluted with saturated aqueous NaCl (20 cm^3) and extracted with ethyl acetate. The extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure to afford an oily residue, which was purified by silica gel column chromatography. The fractions eluted with 30:1–10:1 hexane–ethyl acetate afforded **8a**, **b** and **9** as colourless oils.

Methyl (R)-1-(3-*ethoxycarbonylpropyl*)-2-*oxocyclopentanecarboxylate* **8a**: 90% yield; $[\alpha]_D^{27}$ −25.3 (*c* 0.2 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 1750–1730 (C=O); δ_H(270 MHz; $CDCl_3$) 4.12 (2 H, q, *J* 7), 3.71 (3 H, s), 2.62–2.28 (4 H, m), 2.05–1.89 (4 H, m), 1.71–1.52 (4 H, m), 1.25 (3 H, t, *J* 7); *m/z* (EI) 256 (M^+, 4%), 228 (44), 224 (28) and 142 (100).

Methyl (S)-1-(4-*methoxycarbonylbutyl*)-2-*oxocyclopentanecarboxylate* **8b**: 70% yield; $[\alpha]_D^{30}$ −20.2° (*c* 1.0 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 1740–1730 (C=O); δ_H(270 MHz; $CDCl_3$) 3.70 (3 H, s), 3.66 (3 H, s), 2.57–2.19 (5 H, m), 2.05–1.83 (4 H, m), 1.68–1.51 (3 H, m) and 1.42–1.20 (2 H, m); *m/z* (EI) 256 (M^+, 9%), 224 (10) and 142 (100).

Methyl (R)-1-(4-*methoxycarbonylbutyl*)-2-*oxocyclohexanecarboxylate* **9**: 85% yield; $[\alpha]_D^{24}$ +76.2 (*c* 0.62 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 1740–1710 (C=O); δ_H(270 MHz; $CDCl_3$) 3.73 (3 H, s), 3.66 (3 H, s), 2.53–2.41 (3 H, m), 2.31 (2 H, m), 2.03–1.16 (11 H, m); *m/z* (EI) 270 (M^+, 2%), 239 (20) and 156 (100).

General Procedure for Conversion of the Enol Ethers **4a**, **b** *and* **7** *into the Acetals* **11a**, **b** *and* **14**.—To a solution of the enol ether (368 mg, 1 mmol) in benzene (15 cm^3) was added *p*-TsOH·H_2O (38 mg, 0.2 mmol). The resulting mixture was refluxed with azeotropic removal of water for 0.5 h after which the reaction was quenched with $NaHCO_3$ (504 mg, 6 mmol) and aqueous saturated $NaHCO_3$ (20 cm^3) at 0 °C. The whole was extracted with ethyl acetate. The extracts were dried ($MgSO_4$) and concentrated under reduced pressure to afford an oily residue, which was purified by silica gel column chromatography. The fractions eluted with hexane–ethyl acetate (30:1) afforded the acetals as colourless oils.

Methyl 2′-(3-*ethoxycarbonylpropyl*)*spiro*[(3aR,8aR)-*hexahydrocyclohepta*-1,3-*dioxole*-2,1′-(2′R)-*cyclopentane*]-2′-*carboxylate* **11a**: 92% yield; $[\alpha]_D^{23}$ −32.6 (*c* 0.8 in $CHCl_3$); ν_{max}(neat)/ cm^{-1} 1730br (C=O); δ_H(270 MHz; $CDCl_3$) 4.11 (2 H, q, *J* 7), 3.77 (1 H, m), 3.68 (3 H, s), 3.59 (1 H, m), 2.45–2.27 (3 H, m), 2.21–2.03 (3 H, m), 2.0–1.73 (3 H, m), 1.72–1.45 (13 H, m) and 1.25 (3 H, t, *J* 7); δ_C(100 MHz; $CDCl_3$) 174.0 (s), 173.4 (s), 118.1 (s), 81.6 (d), 81.3 (d), 60.2 (t), 59.1 (s), 55.1 (q), 37.7 (t), 34.7 (t), 32.9 (t), 31.0 (t), 30.3 (t), 28.8 (t), 25.2 (t), 25.0 (t), 24.9 (t), 21.0 (t), 19.7 (t) and 14.3 (q); *m/z* (EI) 368 (M^+, 19%), 267 (18) and 167 (100).

Methyl 2′-(4-*methoxycarbonylbutyl*)*spiro*[(3aR,8aR)-*hexahydrocyclohepta*-1,3-*dioxole*-2,1′-(2′S)-*cyclopentane*]-2′-*carboxylate* **11b**: 87% yield; $[\alpha]_D^{20}$ −24.9 (*c* 1.0 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 1740br (C=O); δ_H(270 MHz; $CDCl_3$) 3.76–3.52 (2 H, m), 3.67 (3 H, s), 3.66 (3 H, s), 2.39–2.27 (3 H, m) and 2.18–1.02 (21 H, m); δ_C(100 MHz; $CDCl_3$) 174.2 (s), 174.0 (s), 118.0 (s), 81.6 (d), 81.3 (d), 59.1 (s), 51.4 (q), 51.4 (q), 37.5 (t), 33.9 (t), 32.9 (t), 31.0 (t), 30.3 (t), 29.7 (t), 28.8 (t), 25.4 (t), 25.2 (t), 25.0 (t), 24.9 (t) and 19.6 (t); *m/z* (EI) 368 (M^+, 19.4%), 267 (23) and 167 (100).

Methyl 2′-(4-*methoxycarbonylbutyl*)*spiro*[(3aS,7aS)-*hexahydro*-1,3-*benzodioxole*-2,1′-(2′R)-*cyclopentane*]-2′-*carboxylate* **14**: 95% yield; $[\alpha]_D^{26}$ −4.6 (*c* 0.75 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 1740br (C=O); δ_H(270 MHz; $CDCl_3$) 3.68 (3 H, s), 3.65 (3 H, s), 3.29 (1 H, m), 3.15 (1 H, m), 2.34–2.28 (2 H, m), 2.20–1.99 (4 H, m) and 1.78–1.01 (18 H, m); δ_C(100 MHz; $CDCl_3$) 174.7 (s), 174.0 (s), 111.1 (s), 80.5 (d), 79.6 (d), 54.9 (s), 51.6 (q), 51.4 (q), 33.8 (t), 33.1 (t), 30.5 (t), 29.7 (t), 28.8 (t), 28.8 (t), 25.3 (t), 24.0 (t), 23.8 (t), 23.8 (t), 23.1 (t) and 20.3 (t); *m/z* (EI) 368 (M^+, 19.0%) and 156 (100).

General Procedure for Dieckmann Condensation of **11a**, **b** *and* **14**.—A solution of lithium bis(trimethylsilyl)amide (1 mol dm^{-3}

THF solution; 5.4 cm^3, 5.4 mmol) was added dropwise to a stirred solution of the substrate (2.7 mmol) in THF (20 cm^3) at 0 °C under an Ar atmosphere. After being stirred for 1 h at room temp., the reaction mixture was diluted with saturated aqueous NH_4Cl, and extracted with ethyl acetate. The extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel. The fraction eluted with hexane–ethyl acetate (30:1–20:1) afforded **12a, b** and **15** as colourless oils.

Ethyl 2″-oxodispiro[(3aR,8aR)-*hexahydrocyclohepta*-1,3-*dioxole*-2,1′-*cyclopentane*-2′,1″-(1″S,3″RS)-*cyclopentane*]-3″-*carboxylate* **12a**: 91% yield; $[\alpha]_D^{27}$ +57.1 (*c* 1.7 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 1750 (C=O), 1730 (C=O), 1655 and 1620; δ_H(270 MHz; $CDCl_3$) 4.25 (2 H, m), 3.66 (2 H, m), 3.33–3.21 (1 H, m), 2.39–2.03 (8 H, m), 1.99–1.46 (12 H, m) and 1.28 (3 H, t, *J* 7); *m/z* (EI) 336 (M^+, 7%), 178 (16) and 167 (100).

Methyl 2″-oxodispiro[(3aR,8aR)-*hexahydrocyclohepta*-1,3-*dioxole*-2,1′-*cyclopentane*-2′,1″-(1″R,3″RS)*cyclohexane*]-3″-*carboxylate* **12b**: 94% yield; $[\alpha]_D^{25}$ +78.6 (*c* 1.1 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 1740 (C=O), 1700 (C=O), 1645 and 1610; δ_H(270 MHz; $CDCl_3$) 3.94–3.57 (3 H, m), 3.75, 3.74 (total 3 H, s each, ratio 2:3) and 2.50–1.19 (22 H, m); *m/z* (EI) 336 (M^+, 16%), 192 (27) and 167 (100).

Methyl 2″-oxodispiro[(3aS,7aS)-*hexahydro*-1,3-*benzodioxole*-2,1′-*cyclohexane*-2′,1″-(1″S)-*cyclohexane*]-3″-*carboxylate* **15**: 94% yield; $[\alpha]_D^{25}$ +78.6 (*c* 1.1 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 1740 (C=O), 1700 (C=O), 1640 and 1605; δ_H(270 MHz; $CDCl_3$) 4.01, 3.61 (total 1 H, dd each, *J* 11, 7 and *J* 13, 7, ratio 3:2), 3.74, 3.73 (total 3 H, s each), 3.42–3.10 (2 H, m) and 2.35–1.14 (22 H, m); *m/z* (EI) 336 (M^+, 70%), 206 (100) and 178 (98).

General Procedure for the Dealkoxycarbonylation of the β-*Keto Esters* **12a, b** *and* **15**.—To a mixture of 2 mol dm^{-3} aqueous KOH (12 cm^3) and MeOH (30 cm^3) was added a solution of substrate (5 mmol) in MeOH (1 cm^3) at room temperature. The reaction mixture was refluxed for 3 h and then diluted with brine (20 cm^3), and extracted with ethyl acetate. The extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure to afford an oily residue, which was purified by silica gel column chromatography. The fraction eluted with 30:1 hexane–ethyl acetate afforded **13a, b** and **16** as colourless oils.

Dispiro [(3aR,8aR)-*hexahydrocyclohepta*-1,3-*dioxole*-2,1′-*cyclopentane*-2′,1″-(1″R)-*cyclopentan*]-2″-*one* **13a**: 90% yield; $[\alpha]_D^{25}$ +63.3 (*c* 0.4 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 1740 (C=O); δ_H(270 MHz; $CDCl_3$) 3.73 (1 H, m), 3.60 (1 H, m), 2.45–2.05 (6 H, m), 2.0–1.70 (6 H, m) and 1.69–1.45 (10 H, m); δ_C(100 MHz; $CDCl_3$) 220.3 (s), 117.9 (s), 81.6 (d), 80.0 (d), 59.9 (s), 38.8 (t), 36.1 (t), 33.3 (t), 32.1 (t), 30.4 (t), 28.7 (t), 25.2 (t), 25.0 (t), 25.0 (t), 19.6 (t) and 19.4 (t); *m/z* (EI) 264 (M^+, 19%), 168 (13) and 167 (100).

Dispiro [(3aR,8aR)-*hexahydrocyclohepta*-1,3-dioxole-2,1′-*cyclopentane*-2′,1″-(1″R)-*cyclohexan*]-2″-*one* **13b**: 90% yield; $[\alpha]_D^{24}$ +61.1 (*c* 1.1 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 1710 (C=O); δ_H(270 MHz; $CDCl_3$) 3.82–3.63 (2 H, m), 2.65 (1 H, m), 2.43–2.09 (5 H, m) and 2.02–1.23 (18 H, m); δ_C(100 MHz; $CDCl_3$) 212.7 (s), 117.4 (s), 81.0 (d), 80.1 (d), 59.8 (s), 41.7 (t), 36.6 (t), 34.4 (t), 33.9 (t), 30.8 (t), 28.7 (t), 26.9 (t), 25.1 (t), 25.1 (t), 25.1 (t), 22.5 (t), and 18.9 (t); *m/z* (EI) 278 (M^+, 11%) and 167 (100).

Dispiro [(3aS,7aS)-*hexahydro*-1,3-*benzodioxole*-2,1′-*cyclohexane*-2′,1″-(1″R)-*cyclohexan*]-2″-*one* **16**: 86% yield; $[\alpha]_D^{26}$ +6.1 (*c* 0.54 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 1705 (C=O); δ_H(270 MHz; $CDCl_3$) 3.39 (1 H, m), 3.14 (1 H, m), 2.42 (2 H, m), 2.29–2.02 (4 H, m) and 2.02–1.23 (18 H, m); δ_C(270 MHz; $CDCl_3$) 213.2 (s), 110.8 (s), 81.1 (d), 79.7 (d), 57.4 (s), 40.4 (t), 33.6 (t), 33.5 (t), 32.9 (t), 29.9 (t), 28.7 (t), 27.1 (t), 23.9 (t), 23.8 (t), 22.9 (t), 21.4 (t) and 20.6 (t); *m/z* (EI) 278 (M^+, 48%), 180 (61) and 152 (100).

(R)-*Spiro*[4.4]*nonane*-1,6-*dione* **1a**.—To a suspended mixture of $ZnBr_2$ (171 mg, 0.76 mmol) and CH_2Cl_2/THF (100:1; 5 cm^3) was added a solution of **13a** (100 mg, 0.38 mmol) in CH_2Cl_2 (1 cm^3) at room temperature. The reaction mixture was stirred for 24 h, after which $ZnBr_2$ (85.5 mg, 0.38 mmol) was added to it. After being stirred for an additional 24 h, the reaction mixture was diluted with saturated aqueous $NaHCO_3$ (20 cm^3), and extracted with ethyl acetate. The extracts were dried ($MgSO_4$) and concentrated under reduced pressure to afford an oily residue, which was then purified by silica gel column chromatography. The fraction eluted with 30:1 hexane–ethyl acetate afforded **1a** (40 mg, 70%) as colourless needles, m.p. 65 °C (methanol); $[\alpha]_D^{26}$ +133 (*c* 0.3 in cyclohexane) {lit.,[4a] for (*S*)-**1a**: $[\alpha]_D^{26}$ −135 (*c* 0.5 in cyclohexane)}; ν_{max}(neat)/cm^{-1} 1739 (C=O); δ_H(270 MHz; $CDCl_3$) 2.48–2.33 (4 H, m), 2.32–2.19 (4 H, m), 2.17–1.78 (4 H, m); δ_C(270 MHz; $CDCl_3$) 216.7 (s), 64.4 (s), 38.5 (t), 34.3 (t) and 19.8 (t); *m/z* (EI) 152 (M^+, 28%) and 97 (100); *m/z* 152.0830 (M^+; Calc. for $C_9H_{12}O_2$ 152.0837).

(R)-*Spiro*[5.5]*undecane*-1,7-*dione* **1c**.—To a solution of **16** (151 mg, 0.54 mmol) in acetone (3 cm^3) was added 3.5% aqueous HCl (1 cm^3). The reaction mixture was stirred at room temp. for 2 h, after which it was diluted with brine (10 cm^3) and extracted with ethyl acetate. The extracts were dried ($MgSO_4$) and concentrated under reduced pressure to afford an oily residue, which was purified by silica gel column chromatography. The fraction eluted with 30:1 hexane–ethyl acetate afforded **1c** (94 mg, 96%) as a colourless oil; $[\alpha]_D^{27}$ +114 (*c* 0.3 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 1700 (C=O); δ_H(270 MHz; $CDCl_3$) 2.56–2.36 (6 H, m), 1.98–1.66 (8 H, m) and 1.60–1.43 (2 H, m); δ_C(270 MHz; $CDCl_3$) 210.8 (s), 64.5 (s), 40.8 (t), 36.2 (t), 27.7 (t) and 21.3 (t); *m/z* (EI) 180 (M^+, 100%), 152 (77); *m/z* 180.1140 (M^+; Calc. for $C_{11}H_{16}O_2$ 180.1150).

General Procedure for DIBAL-H Reduction of the Keto Acetals **13a, b**.—To a solution of **13a, b** (1 mmol) in THF (5 cm^3) was added DIBAL-H (1 mol dm^{-3} in THF; 2 cm^3, 2 mmol) at −78 °C, and the resulting mixture was stirred for 3 h at −70 to −60 °C. Work-up of the mixture and purification of the residue by silica gel column chromatography (30:1 hexane–ethyl acetate) afforded **17a, b** as colourless oils.

Dispiro [(3aR,8aR)-*hexahydrocyclohepta*-1,3-*dioxole*-2,1′-*cyclopentane*-2′,1″-(1″R,2″R)-*cyclopentan*]-2″-*ol* **17a**: 98% yield; $[\alpha]_D^{22}$ −33.0 (*c* 1.1 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 3500 (OH); δ_H(270 MHz; $CDCl_3$) 4.38 (1 H, s, OH), 3.98 (1 H, d, *J* 3), 3.83–3.71 (2 H, m), 2.24–2.14 (2 H, m), 2.11–1.77 (5 H, m) and 1.73–1.43 (15 H, m); δ_C(100 MHz; $CDCl_3$) 118.9 (s), 82.0 (d), 79.7 (d), 78.9 (d), 56.8 (s), 36.1 (t), 34.6 (t), 33.1 (t), 30.5 (t), 29.8 (t), 28.7 (t), 25.2 (t), 24.9 (t), 24.9 (t), 20.2 (t) and 18.4 (t); *m/z* (EI) 266 (M^+, 14%), 248 (17) and 95 (100).

Dispiro [(3aR,8aR)-*hexahydrocyclohepta*-1,3-*dioxole*-2,1′-*cyclopentane*-2,1″-(1″R,2″R)-*cyclohexan*]-2″-*ol* **17b**: 86% yield; $[\alpha]_D^{23}$ −50.9 (*c* 1.45 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 3500 (OH); δ_H(270 MHz; $CDCl_3$) 4.17 (1 H, s, OH), 3.91 (1 H, dd, *J* 2, 1), 3.82–3.69 (2 H, m), 2.21–2.12 (2 H, m) and 1.99–1.22 (22 H, m); δ_C(100 MHz; $CDCl_3$) 119.9 (s), 81.7 (d), 80.2 (d), 70.7 (d), 48.3 (s), 34.4 (t), 31.1 (t), 30.5 (t), 29.1 (t), 28.7 (t), 25.3 (t), 25.1 (t), 24.9 (t), 24.9 (t), 22.2 (t), 19.5 (t) and 17.7 (t); *m/z* (EI) 280 (M^+, 25%), 262 (16) and 167 (100).

Dispiro [(3aS,7aS)-*hexahydro*-1,3-*benzodioxole*-2,1′-*cyclohexane*-2,1″-(1″R,2″R)-*cyclohexan*]-2″-*ol* **17c**.—To a suspended solution of $LiAlH_4$ (152 mg, 4 mmol) in THF (15 cm^3) was added dropwise a solution of **16** (278 mg, 1 mmol) in THF (3 cm^3) at −50 °C. The resulting mixture was stirred for 2 h, after which the reaction was quenched by the addition of ethyl acetate (1 cm^3) and saturated aqueous NH_4Cl (0.2 cm^3) to the

mixture; the resulting precipitate was filtered off. The filtrate was dried ($MgSO_4$) and concentrated under reduced pressure to afford an oily residue, which was purified by silica gel column chromatography. The fraction eluted with 30:1 hexane–ethyl acetate afforded **17c** (263 mg, 94%) of 96% d.e. as a colourless oil; $[\alpha]_D^{27}$ +9.0 (*c* 0.62 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 3480 (OH); δ_H(270 MHz; $CDCl_3$) 4.26 (1 H, s), 4.13 (1 H, s, OH), 3.39 (1 H, m), 3.23 (1 H, m), 2.15–2.03 (3 H, m) and 1.96–1.17 (21 H, m); δ_C(100 MHz; $CDCl_3$) 113.8 (s), 81.0 (d), 79.9 (d), 68.7 (d), 44.1 (s), 32.3 (t), 31.1 (t), 29.7 (t), 28.5 (t), 27.8 (t), 24.9 (t), 23.8 (t), 23.8 (t), 23.1 (t), 20.2 (t), 19.9 (t) and 19.1 (t); *m/z* (EI) 280 (M^+, 36%), 262 (7) and 164 (100).

General Procedure for the Deacetalization of **17a–c**.—To a solution of **17a–c** (1 mmol) in THF (3 cm^3) was added 3.5% HCl (1 cm^3). The reaction mixture was stirred for 0.5 h at room temp. and then diluted with saturated aqueous NaCl (10 cm^3) and extracted with ethyl acetate. The extracts were dried ($MgSO_4$) and concentrated under reduced pressure to afford an oily residue, which was purified by silica gel column chromatography to afford the hydroxy ketones **18a–c** as colourless oils.

(5R,6R)-6-*Hydroxyspiro*[4.4]*nonan*-1-*one* **18a**: 98% yield; $[\alpha]_D^{22}$ +47.7 (*c* 2.0 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 3450 (OH) and 1725 (C=O); δ_H(270 MHz; $CDCl_3$) 4.00 (1 H, dd, *J* 4, 3), 3.44 (1 H, d, *J* 4, OH), 2.39–2.27 (2 H, m), 2.08–1.75 (8 H, m) and 1.74–1.57 (2 H, m); δ_C(100 MHz; $CDCl_3$) 225.1 (s), 80.5 (d), 58.9 (s), 39.0 (t), 35.7 (t), 34.5 (t), 33.9 (t), 21.4 (t) and 19.3 (t); *m/z* (EI) 154 (M^+, 28%), 136 (25) and 97 (100); *m/z* 154.0987 (M^+; Calc. for $C_9H_{14}O_2$ 154.0994).

(5R,6R)-6-*Hydroxyspiro*[4.5]*decan*-1-*one* **18b**: 88% yield; $[\alpha]_D^{23}$ +24.4 (*c* 2.0 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 3450 (OH) and 1720 (C=O); δ_H(270 MHz; $CDCl_3$), 3.78 (1 H, s, OH), 3.68 (1 H, dd, *J* 3, 2), 2.45–2.00 (2 H, m), 2.08–1.56 (8 H, m) and 1.49–1.25 (4 H, m); δ_C(100 MHz; $CDCl_3$) 225.9 (s), 71.0 (d), 51.8 (s), 38.5 (t), 32.8 (t), 29.0 (t), 27.1 (t), 20.9 (t), 19.8 (t) and 18.8 (t); *m/z* (EI) 168 (M^+, 36%), 150 (61) and 97 (100); *m/z* 168.1142 (M^+; Calc. for $C_{10}H_{16}O_2$ 168.1150).

(6R,7R)-7-*Hydroxyspiro*[5.5]*undecan*-1-*one* **18c**: 94% yield; $[\alpha]_D^{26}$ −59.8 (*c* 0.62 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 3470 (OH) and 1700 (C=O); δ_H(270 MHz; $CDCl_3$) 3.42 (1 H, m), 3.21 (1 H, d, *J* 7, OH), 2.57 (1 H, m), 2.28–2.17 (2 H, m) and 2.08–1.14 (13 H, m); δ_C(100 MHz; $CDCl_3$) 219.6 (s), 74.2 (d), 53.7 (s), 39.4 (t), 36.2 (t), 30.9 (t), 30.1 (t), 28.3 (t), 22.6 (t), 21.3 (t) and 20.4 (t); *m/z* (EI) 182 (M^+, 29%), 164 (64) and 111 (100); *m/z* 182.1301 (M^+, Calc. for $C_{11}H_{18}O_2$ 182.1307).

(R)-*Spiro*[4.5]*decane*-1,6-*dione* **1b**.—To a mixture of **18b** (220 mg, 1.31 mmol), CCl_4 (1.5 cm^3), MeCN (1.5 cm^3) and water (2.5 cm^3) was added RuO_2 (5 mg, 0.03 mmol) and $NaIO_4$ (400 mg, 1.87 mmol) at room temperature. After being stirred for 24 h, the reaction mixture was extracted with CH_2Cl_2. The extracts were dried ($MgSO_4$) and concentrated under reduced pressure to afford an oily residue, which was purified by silica gel column chromatography. The fraction eluted with 10:1 hexane–ethyl acetate afforded **1b** (167 mg, 77%) as a colourless oil; $[\alpha]_D^{23}$ +198 (*c* 0.4 in $CHCl_3$) {lit.,[4c] $[\alpha]_D$ +185 (*c* 0.4 in $CHCl_3$)}; ν_{max}(neat)/cm^{-1} 1740 (C=O) and 1700 (CO); δ_H(270 MHz; $CDCl_3$) 2.75–2.63 (2 H, m), 2.44 (1 H, m), 2.34–2.28 (2 H, m) and 2.19–1.53 (9 H, m); δ_C(270 MHz; $CDCl_3$) 215.6 (s), 208.0 (s), 64.4 (s), 39.8 (t), 38.6 (t), 36.0 (t), 33.8 (t), 26.7 (t), 21.1 (t) and 19.1 (t); *m/z* (EI) 166 (M^+, 60%), 138 (29) and 111 (100); *m/z* 166.0988 (M^+; Calc. for $C_{10}H_{14}O_2$ 166.0994).

General Procedure for TBDPS Protection of **18a–c**.—To a mixture of **18** (1 mmol) and imidazole (272 mg, 4 mmol) was added a solution of *tert*-butyl(chloro)diphenylsilane (550 mg, 2 mmol) in DMF (2 cm^3) at room temperature. After being stirred for 48 h, the reaction mixture was diluted with saturated aqueous $NaHCO_3$ (20 cm^3), and extracted with ethyl acetate. The extracts were dried ($MgSO_4$) and concentrated under reduced pressure to afford an oily residue, which was purified by silica gel column chromatography. The fraction eluted with 50:1 hexane–ethyl acetate afforded **20** as a colourless oil.

(5R,6R)-6-tert-*Butyldiphenylsiloxyspiro*[4.4]*nonan*-1-*one* **20a**: 95% yield; $[\alpha]_D^{23}$ −14.6 (*c* 2.1 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 1740 (CO); δ_H(270 MHz; $CDCl_3$) 7.77–7.65 (4 H, m), 7.45–7.35 (6 H, m), 4.05 (1 H, t, *J* 6), 2.31–2.15 (2 H, m), 2.12–1.92 (3 H, m), 1.89–1.72 (4 H, m), 1.57–1.23 (3 H, m) and 1.02 (9 H, s); δ_C(100 MHz; $CDCl_3$) 220.5 (s), 135.9 (d), 134.2 (s), 133.6 (s), 129.7 (d), 129.6 (d), 127.6 (d), 127.4 (d), 83.1 (d), 58.8 (s), 39.0 (t), 36.8 (t), 33.9 (t), 33.1 (t), 26.9 (q), 21.0 (t), 19.6 (t) and 19.2 (s); *m/z* (EI) 392 (M^+, 0.1%) and 335 [M^+ − $C(Me)_3$, 100].

(5R,6R)-6-tert-*Butyldiphenylsiloxyspiro*[4.5]*decan*-1-*one* **20b**: 88% yield; $[\alpha]_D^{25}$ +0.14 (*c* 2.0 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 1735 (CO); δ_H(270 MHz; $CDCl_3$) 7.72–7.64 (4 H, m), 7.46–7.32 (6 H, m), 3.55 (1 H, dd, *J* 11, 5), 2.53 (1 H, m), 2.31–0.88 (13 H, m) and 1.01 (9 H, s); δ_C(100 MHz; $CDCl_3$) 220.6 (s), 135.9 (d), 134.7 (s), 133.5 (s), 129.6 (d), 129.3 (d), 127.6 (d), 127.2 (d), 76.5 (d), 52.5 (s), 40.7 (t), 36.2 (t), 32.9 (t), 30.5 (t), 27.1 (q), 24.0 (t), 20.7 (t), 19.4 (s) and 19.0 (t); *m/z* (EI) 406 (M^+, 0.08%), 350 (31) and 349 [M^+ − $C(Me)_3$, 100].

(6R,7R)-7-tert-*Butyldiphenylsiloxyspiro*[5.5]*undecan*-1-*one* **20c**: 78% yield; $[\alpha]_D^{29}$ −6.2 (*c* 2.0 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 1700 (CO); δ_H(270 MHz; $CDCl_3$) 7.70–7.63 (4 H, m), 7.46–7.32 (6 H, m), 4.10 (1 H, m), 2.35–2.24 (2 H, m), 2.11–0.85 (14 H, m) and 1.02 (9 H, s); δ_C(100 MHz; $CDCl_3$) 213.9 (s), 136.1 (d), 135.7 (s), 134.7 (s), 129.6 (d), 129.5 (d), 127.5 (d), 127.2 (d), 73.3 (d), 53.4 (s), 39.4 (t), 36.1 (t), 29.5 (t), 28.9 (t), 27.8 (t), 27.0 (q), 21.1 (t), 20.7 (t), 20.4 (t) and 19.3 (s); Ms *m/z* (EI) 363 [M^+ − $C(Me)_3$, 100] and 279 (55).

Diastereoselective Reduction of **20** *to* **21**.—Compounds **20** were reduced with DIBAL-H at −60 °C in a manner similar to that described for the preparation of **18**.

(1R,5R,6R)-6-tert-*Butyldiphenylsiloxyspiro*[4.4]*nonan*-1-*ol* **21a**: 85% yield; $[\alpha]_D^{25}$ −34.8 (*c* 0.5 in $CHCl_3$); ν_{max}(neat)/ cm^{-1} 3500 (OH); δ_H(270 MHz; $CDCl_3$) 7.75–7.65 (4 H, m), 7.48–7.38 (6 H, m), 4.21 (1 H, d, *J* 4), 4.17 (1 H, t, *J* 5), 3.95 (1 H, s, OH), 1.89–1.80 (2 H, m), 1.74–1.49 (6 H, m), 1.45–1.15 (4 H, m) and 1.07 (9 H, s); δ_C(100 MHz; $CDCl_3$) 135.9 (d), 134.0 (s), 133.0 (s), 129.9 (d), 129.8 (d), 127.8 (d), 127.6 (d), 81.8 (d), 78.9 (d), 58.0 (s), 33.9 (t), 33.1 (t), 32.9 (t), 32.9 (t), 27.0 (q), 21.0 (t), 19.9 (t) and 19.0 (s); *m/z* (EI) 393 (M^+ − 1, 0.05%), 376 (0.1), 337 (16) and 121 (100).

(1S,5R,6R)-6-tert-*Butyldiphenylsiloxyspiro*[4.4]*nonan*-1-*ol* **22a**: 9% yield; ν_{max}(neat)/cm^{-1} 3500 (OH); δ_H(270 MHz; $CDCl_3$) 7.78–7.70 (4 H, m), 7.47–7.35 (6 H, m), 4.36 (1 H, t, *J* 7), 3.79 (1 H, s), 2.78 (1 H, d, *J* 3, OH), 2.26 (1 H, m), 1.96–1.74 (2 H, m), 1.72–1.53 (3 H, m), 1.48–1.38 (4 H, m), 1.37–1.19 (2 H, m) and 1.07 (9 H, s); *m/z* (EI) 394 (M^+, 0.02%), 393 (M^+ − 1, 0.04%), 376 (0.8), 337 (16), 199 (100) and 121 (98).

(1R,5R,6R)-6-tert-*Butyldiphenylsiloxyspiro*[4.5]*decan*-1-*ol* **21b**: 70% yield; $[\alpha]_D^{26}$ −20.3 (*c* 1.53 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 3480 (OH); δ_H(270 MHz; $CDCl_3$) 7.74–7.65 (4 H, m), 7.50–7.34 (6 H, m), 4.23 (1 H, s), 4.02 (1 H, br s, OH), 3.72 (1 H, dd, *J* 9, 3), 2.04 (1 H, m), 1.92–1.01 (12 H, m), 1.08 (9 H, s) and 0.92 (1 H, m); δ_C(100 MHz; $CDCl_3$) 136.0 (d), 133.9 (s), 132.7 (s), 130.1 (d), 129.7 (d), 127.8 (d), 127.5 (d), 78.0 (d) 77.8 (d), 51.4 (s), 34.0 (t), 33.7 (t), 32.7 (t), 32.2 (t), 27.1 (q), 23.6 (t), 21.8 (t), 20.9 (t) and 19.4 (s); *m/z* (FD) 409 (M^+ + 1, 7.0%), 352 [M^+ − $C(Me)_3$, 40] and 351 (100).

(1R,6R,7R)-7-tert-*Butyldiphenylsiloxyspiro*[5.5]*undecan*-1-*ol* **21c**: 67% yield; $[\alpha]_D^{28}$ −23.6 (*c* 1.0 in $CHCl_3$); ν_{max}(neat)/ cm^{-1} 3550 (OH); δ_H(270 MHz; $CDCl_3$) 7.75–7.66 (4 H, m), 7.49–7.35 (6 H, m), 4.65 (1 H, br s, OH), 4.35 (1 H, br s), 3.42

(1 H, dd, *J* 10, 4), 2.37–2.24 (1 H, m), 2.06–0.84 (14 H, m), 1.08 (9 H, s) and 0.78 (1 H, m); δ_C(100 MHz; $CDCl_3$) 136.1 (d), 136.0 (d), 133.9 (s), 132.3 (s), 130.0 (d), 129.7 (d), 127.7 (d), 127.4 (d), 82.2 (d), 68.9 (d), 40.5 (s), 31.9 (t), 30.6 (t), 30.1 (t), 28.4 (t), 27.1 (q), 24.3 (t), 20.6 (t), 20.2 (t), 19.8 (t) and 19.4 (s); *m/z* (FD) 365 [$M^+ - C(Me)_3$, 26], 199 (87) and 149 (100).

General Procedure for the Deprotection of **21**.—To a solution of **21** (1 mmol) in THF (2 cm^3) was added tetrabutylammonium fluoride (1 mol dm^{-3} in THF; 2 cm^3, 2 mmol). The mixture was stirred at room temp. for 2 h after which it was diluted with brine (4 cm^3), and extracted with ethyl acetate. The extracts were dried ($MgSO_4$), and concentrated under reduced pressure to afford an oily residue, which was purified by silica gel column chromatography. The fraction eluted with 3:1 hexane–ethyl acetate afforded **2** as a colourless oil.

(1R,5R,6R)-*Spiro*[4.4]*nonane*-1,6-*diol* **2a**: 99% yield; $[\alpha]_D^{26}$ −100.7 (*c* 1.2 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 3350 (OH); δ_H(270 MHz; $CDCl_3$) 4.14 (2 H, dd, *J* 5, 3), 2.73 (2 H, br s), 1.98–1.81 (4 H, m), 1.73–1.58 (6 H, m) and 1.38–1.25 (2 H, m); δ_C(100 MHz; $CDCl_3$) 79.6 (d), 58.3 (s), 34.3 (t), 33.9 (t) and 21.2 (t); *m/z* (EI) 156 (M^+, 0.05%), 154 (0.1), 138 (1.5) and 94 (100); *m/z* 156.1142 (M^+; Calc. for $C_9H_{16}O_2$ 156.1150).

(1R,5R,6R)-*Spiro*[4.5]*decane*-1,6-*diol* **2b**: 99% yield; $[\alpha]_D^{22}$ −65.5 (*c* 1.6 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 3400 (OH); δ_H(270 MHz; $CDCl_3$) 4.02 (1 H, dd, *J* 5, 2), 3.84 (1 H, dd, *J* 5, 3), 2.67 (2 H, br s) and 2.00–1.05 (14 H, m); δ_C(100 MHz; $CDCl_3$) 80.6 (d), 72.9 (d), 49.6 (s), 33.6 (t), 32.6 (t), 31.1 (t), 22.2 (t), 21.6 (t) and 21.4 (t); *m/z* (EI) 170 (M^+, 1%), 168 (7), 152 (10), 134 (98) and 108 (100); *m/z* 170.1314 (M^+; Calc. for $C_{10}H_{18}O_2$ 170.1307).

(1R,6R,7R)-*Spiro*[5.5]*undecane*-1,7-*diol* **2c**: 88% yield; $[\alpha]_D^{28}$ −44.6 (*c* 0.2 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 3320 (OH); δ_H(270 MHz; $CDCl_3$) 3.87 (2 H, d, *J* 6), 2.93 (2 H, br s), 2.17–1.96 (2 H, m), 1.76–1.57 (8 H, m), 1.49–1.37 (4 H, m) and 1.12–1.03 (2 H, m); δ_C(100 MHz; $CDCl_3$) 74.1 (d), 39.8 (s), 30.7 (t), 29.5 (t), 22.0 (t) and 20.5 (t); *m/z* (EI) 185 ($M^+ + 1$, 16%), 184 (M^+, 14%) and 166 (100); *m/z* 184.1455 (M^+; Calc. for $C_{11}H_{20}O_2$ 184.1463).

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